Claims

1. A method for enhancing specifically the cytotoxicity or proliferation of killer T cells in a subject, comprising:

administering to a subject in need of such treatment an agent that selectively reduces cross-linking of biliary glycoprotein polypeptides in an amount effective to enhance the cytotoxicity or proliferation of killer T cells in the subject.

2. The method of claim 1, wherein the agent is an antibody or antibody fragment which binds only a single biliary glycoprotein polypeptide.

3. The method of claim 2, wherein the antibody fragment is a Fab fragment.

4. The method of claim 1, wherein the agent comprises a ligand for the biliary glycoprotein polypeptide, wherein the ligand binds only a single biliary glycoprotein polypeptide.

5. The method of claim 4, wherein the ligand is fused to an immunoglobulin molecule or a fragment thereof.

6. The method of claim 4, wherein the ligand is a soluble biliary glycoprotein molecule or fragment thereof.

7. The method of claim 1, wherein the killer T cells are selected from the group consisting of $CD4^+$ T cells, $CD8^+$ T cells and NK cells.

8. The method of claim 1, wherein the killer T cells are intestinal intraepithelial lymphocytes.

9. The method of claim 1, wherein the killer T cells are peripheral blood T cells.

10. A method for suppressing specifically the cytotoxicity or proliferation of killer T cells in a subject, comprising:

administering to a subject in need of such treatment an agent that selectively increases cross-linking of biliary glycoprotein polypeptides in an amount effective to suppress the activity of killer T cells in the subject.

11. The method of claim 10, wherein the agent is an antibody.

12. The method of claim 11, wherein the antibody is a monoclonal antibody.

13. The method of claim 10, wherein the agent comprises a ligand for the biliary glycoprotein polypeptide, wherein the ligand binds two or more biliary glycoprotein polypeptides.

14. The method of claim 13,wherein the ligand is fused to an immunoglobulin molecule or a fragment thereof.

15. The method of claim 13, wherein the ligand comprises a biliary glycoprotein polypeptide or fragment thereof.

16. The method of claim 10, wherein the killer T cells are selected from the group consisting of $CD4^+$ T cells, $CD8^+$ T cells and NK cells.

17. The method of claim 10, wherein the killer T cells are intestinal intraepithelial lymphocytes.

18. The method of claim 10, wherein the killer T cells are peripheral blood T cells.

19. A composition comprising

an agent that selectively selectively reduces cross-linking of biliary glycoprotein polypeptides in an amount effective to enhance cytotoxicity or proliferation of killer T cells in a subject, and

a pharmaceutically-acceptable carrier.

20. The composition of claim 19, wherein the agent is an antibody or antibody fragment which binds only a single biliary glycoprotein molecule.

21. The composition of claim 20, wherein the antibody fragment is a Fab fragment.

22. The composition of claim 19, wherein the agent comprises a ligand for the biliary glycoprotein polypeptide, wherein the ligand binds only a single biliary glycoprotein polypeptide..

23. The composition of claim 22, wherein the ligand is fused to an immunoglobulin molecule or a fragment thereof.

24. The composition of claim 22, wherein the ligand is biliary glycoprotein or a fragment thereof.

25. A composition comprising:

an agent that selectively increases cross-linking of biliary glycoprotein polypeptides in an amount effective to suppress cytotoxicity or proliferation of killer T cells in a subject, and

a pharmaceutically-acceptable carrier.

26. The composition of claim 25, wherein the agent is an antibody.

27. The composition of claim 26, wherein the antibody is a monoclonal antibody.

28. The composition of claim 25, wherein the agent comprises a ligand for the biliary glycoprotein polypeptide, wherein the ligand binds two or more biliary glycoprotein polypeptides.

29. The composition of claim 28, wherein the ligand is fused to an immunoglobulin molecule or a fragment thereof.

30. The composition of claim 28, wherein the ligand is biliary glycoprotein or a fragment

thereof.

31. A method for enhancing specifically cytotoxicity or proliferation of killer T cells, comprising:

contacting a population of killer T cells with an agent that selectively reduces cross-linking of biliary glycoprotein polypeptides in an amount effective to enhance the cytotoxicity or proliferation of the killer T cells.

32. The method of claim 31, wherein the agent is an antibody or antibody fragment that binds one biliary glycoprotein molecule.

33. The method of claim 32, wherein the antibody fragment is a Fab fragment.

34. The method of claim 31, wherein the agent comprises a ligand for the biliary glycoprotein polypeptide which binds only a single biliary glycoprotein polypeptide.

35. The method of claim 34, wherein the ligand is fused to an immunoglobulin molecule or a fragment thereof.

36. The method of claim 34, wherein the ligand is a soluble biliary glycoprotein molecule or a fragment thereof.

37. The method of claim 31, wherein the killer T cells are selected from the group consisting of $CD4^+$ T cells, $CD8^+$ T cells and NK cells.

38. The method of claim 31, wherein the killer T cells are intestinal intraepithelial lymphocytes.

39. The method of claim 31, wherein the killer T cells are peripheral blood T cells.

40. A method for suppressing specifically cytotoxicity or proliferation of killer T cells, comprising:

contacting a population of killer T cells with an agent that selectively increases cross-linking of biliary glycoprotein polypeptides in an amount effective to suppress the cytotoxicity or proliferation of the killer T cells.

41. The method of claim 40, wherein the agent is an antibody.

42. The method of claim 41, wherein the antibody is a monoclonal antibody.

43. The method of claim 40, wherein the agent comprises a ligand for the biliary glycoprotein polypeptide, wherein the ligand binds two or more biliary glycoprotein polypeptides.

44. The method of claim 43, wherein the ligand is fused to an immunoglobulin molecule or a fragment thereof.

45. The method of claim 43, wherein the ligand comprises a soluble biliary glycoprotein molecule or a fragment thereof.

46. The method of claim 40, wherein the killer T cells are selected from the group consisting of $CD4^+$ T cells, $CD8^+$ T cells and NK cells.

47. The method of claim 40, wherein the killer T cells are intestinal intraepithelial lymphocytes.

48. The method of claim 40, wherein the killer T cells are peripheral blood T cells.

49. An isolated fusion protein comprising a biliary glycoprotein polypeptide or a fragment thereof fused to an immunoglobulin molecule or a fragment thereof.

50. The isolated fusion protein of claim 49, wherein the biliary glycoprotein or fragment thereof selectively binds a monoclonal antibody selected from the group consisting of 34B1, 5F4 and 26H7.

51. The isolated fusion protein of claim 50, wherein the fragment of biliary glycoprotein is selected from the group consisting of the N-domain of CD66a, NA1B1 domains of CD66a, the NA1B1A2 domains of CD66a.

52. The isolated fusion protein of claim G1, wherein the fragment of the immunoglobulin molecule is the Fc portion of the immunoglobulin molecule.

53 An isolated fusion protein comprising two or more biliary glycoprotein polypeptides or fragments thereof which bind biliary glycoprotein.

54. A method for identifying compounds which enhance or suppress killer T cell activity, comprising,

(a) contacting a population of killer T cells which express biliary glycoprotein with a compound that binds biliary glycoprotein, and

(b) determining the cytotoxicity or proliferation of the population of killer T cells relative to a control, wherein compounds which increase the cytotoxicity or proliferation are compounds which enhance the killer T cell activity, and wherein compounds which decrease the cytotoxicity or proliferation are compounds which suppress the killer T cell activity.

55. The method of claim 54, further comprising the steps of

(a) providing a biliary glycoprotein polypeptide or a fragment thereof,

(b) contacting the biliary glycoprotein polypeptide or a fragment thereof with a compound,

(c) determining the binding of the compound to the biliary glycoprotein polypeptide or a fragment thereof, wherein the compound is used in step (a) of claim H1.

56. A method for selectively treating a subject having a condition characterized by aberrant killer T cell activity comprising,

administering to a subject in need of such treatment a pharmacological agent which is selective for biliary glycoprotein, in an amount effective to normalize the aberrant killer T cell activity.

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